CLAIMS

1.- Genetic sequence corresponding to SEQ ID NO:1 comprising at least one of the following mutations: (-23)A>C, 1054 del11, 108delC, 1197de19, 1207de1T, 1432delG, 191-2delAinsCT, 2184delG, 231delC, 2399del5ins4, 313+linsT, 338dell6, 509insC, 675dell5, 684dup12, 941-39>T, C195R, C255G, C319Y, D157G, D630N, E291X, H635N, N59K, T41M, W515X, Y379X, Y421X, T433N, 818de18, 1423delGC/insA, 1204insT, 451de13, G516X, 2389+4A>G, 1815del11, 1186+5G>A, T740M, I771T, R279G, T446I, H562Q, C74Y, D686Y, G(-2)R, E579D, S205C, D200V, V766E, L(-6)P, 2544insC, C42Y, 2389+3A>C, [1587-5de15;1587del31], of application in extracorporeal and in vitro diagnostic methods for familial hypercholesterolemia.

2.- Genetic sequence according to claim 1, furthermore comprising any of the following mutations: 2393del9, (-42)C>G, (-49)C>T, 1045delC, 1061-8 T>C, A378T, C358R, 1358+1G>A, 1706-10G>A, 1845+1G>C, 2085del19, 2lldelG, 2140+5G>A, 2207insT, 2390-1G>C, 313+1G>C, 313+1G>A, 518delG, 7delC, 872delC, 884delT, 920ins4, A519T, C113W, C255X, C281Y, C297F, C347Y, C371X, C646Y, C677Y, C68W, C74G, C95R, D151N, D200G, D200Y, D280G, E10X, E246A, E256K, F634L, G322S, G352D, G571E, N543H, N804K, Q12X, Q133X, Q357P, Q427X, Q71E, R395Q, R574W, R612C, S156L, S205P, T413K, T7051, V502M, W(-18)X, W541X, D679E, 1359-1G>A, C127R, 681ins21, C122X, V408M, G528D, D412H, N619N, E80K, L534P, L621S, C356Y, R329X, G248D, C201Y, 313+5G>A, C358Y, C331R, D157N, V776M, P664L, W462X, Q328X, L584P, R395W, G314V, W469X, P678L, R612H, R236W, of application in extra-corporeal and in vitro diagnostic methods, of familial hypercholesterolemia.

3.- Gene sequence according to either of claims 1 or 2 comprising, moreover, any of the following polymorphisms: 81T>C BstUI Exon 2, 1060+10G>C SmaI Exon 7, 1171G>A StuI Exon 8, 1413G>A DdeI Exon 10, 1617C>T BstNI Exon 11, 1725C>T SSCP Exon 12, 1771C>T HincII Exon 12, 1959 T>C AvaII Exon 13, 2232G>A MspI Exon 15, of

application in extra-corporeal and in vitro diagnostic methods, of familial hypercholesterolemia.

4.- Use of the gene sequence of claim 1 in the design and preparation of oligonucleotides capable of hybridising with any of the following mutations:
(-23)A>C, 1054del11, 108delC, 1197del19, 1207del1T, 1432delG, 191-2delAinsCT, 2184del1G, 231delC, 2399del5/ins4, 313+1insT, 338del16, 509insC, 675del15, 684dup12, 941-39 C>T, C195R, C255G, C319Y, D157G, D630N, E291X, H635N, N59K, T41M, W515X, Y379X, Y421X, T433N, 818de18, 1423delGC/insA, 1204insT, 451de13, G516X, 2389+4A>G, 1815del11, 1186+5G>A, T740M, I771T, R279G, T446I, H562Q, C74Y, D686Y, G(-2)R, E579D, S205C, D200V, V766E, L(-6)P, 2544insC, C42Y, 2389+3A>C, [1587-5de15;1587del31].

5.- Oligonucleotide probes capable of hybridising with any of the mutations comprised in the gene sequence of claim 1.

6.- Oligonucleotide probes according to claim 5 selected from between at least one of the following SEQ ID NO:8, SEQ ID NO:11, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:24, SEQ ID NO:29, or at least one from between SEQ ID NO:37 to SEQ ID NO:147 or from between SEQ ID NO:154 to SEQ ID NO:259.

7.- Use of the oligonucleotide probes of claim 5 in an extracorporeal method of in vitro detection of LDL-r gene mutations, for the diagnosis of familial hypercholesterolemia.

8.- Use of the probes of claim 6 in an extracorporeal method of in vitro detection of LDL-r gene mutations, for the diagnosis of familial hypercholesterolemia.

9.- Assay kit comprising a support to which any of the oligonucleotide probes of claim 5 are coupled, of application in the diagnosis of familial hypercholesterolemia.

10.- Assay kit comprising a support to which any of the oligonucleotide probes of claim 6 are coupled, of application in the diagnosis of familial hypercholesterolemia.

11.- Use of any of the oligonucleotide probes selected between: SEQ ID NO: 2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO: 9, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:153 in an extracorporeal method of in vitro detection of LDL-r gene mutations for the diagnosis of familial hypercholesterolemia.

12.- Assay kit according to either of claims 9 or 10 comprising a support to which moreover any of the oligonucleotide probes are coupled selected from between: SEQ ID NO: 2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO: 9, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153 of application in the diagnosis of familial hypercholesterolemia.

13.- Extracorporeal method of in vitro diagnosis of familial hypercholesterolemia, characterized in that in a biological sample of an individual some of the SEQ ID NO:1 mutations, described in claim 1, are detected.

14.- Extracorporeal method of in vitro diagnosis of familial hypercholesterolemia, characterized in that in a biological sample of an individual some of the SEQ ID NO:1 mutations, described in claim 1, in combination with some of the mutations of said SEQ ID NO:1, described in claim 2, are detected.

15.- Extracorporeal method of in vitro diagnosis of familial hypercholesterolemia, characterized in that in a biological sample of an individual some of the SEQ ID NO:1 mutations, described in claim 1, in combination with some of the polymorphisms of said SEQ ID NO:1, described in claim 3, are detected.

16.- Method of diagnosis according to claims 13 to 15, comprising amplifying DNA fragments that contain the mutations of claim 1, alone or in combination with the mutations of claim 2 and/or the polymorphisms of claim 3, by the technique of the chain reaction of the polymerase (PCR), utilizing therefor any of the oligonucleotides selected between SEQ ID NO:2 to SEQ ID NO:259 or combinations of the same, subjecting the PCR products to an analysis by the simple chain conformation polymorphisms technique (SSCP), sequencing those fragments having an anomalous pattern by SSCP to detect the mutations that would be identified subsequently by restriction analysis or by means of the assay kit of claims 9, 10 or 12.